```
   1 cgcggccgcgtcgaccgaaaccaggagccgcgggtgttggcgcaaaggttactcccagac
  61 ccttttccggctgacttctgagaaggttgcgcagcagctgtgcccgacagtctagaggcg
 121 cagaagaggaagccatcgcctggccccggctctctggaccttgtctcgctcgggagcgga
 181 aacagcggcagccagagaactgttttaatcatggacaaacaaaactcacagatgaatgct
   1                                 M  D  K  Q  N  S  Q  M  N  A
 241 tctcacccggaaacaaacttgccagttgggtatcctcctcagtatccaccgacagcattc
  11 S  H  P  E  T  N  L  P  V  G  Y  P  P  Q  Y  P  P  T  A  F
 301 caaggacctccaggatatagtggctaccctgggccccaggtcagctacccaccccacca
  31 Q  G  P  P  G  Y  S  G  Y  P  G  P  Q  V  S  Y  P  P  P  P
 361 gccggccattcaggtcctggcccagctggctttcctgtcccaaatcagccagtgtataat
  51 A  G  H  S  G  P  G  P  A  G  F  P  V  P  N  Q  P  V  Y  N
 421 cagccagtatataatcagccagttggagctgcaggggtaccatggatgccagcgccacag
  71 Q  P  V  Y  N  Q  P  V  G  A  A  G  V  P  W  M  P  A  P  Q
 481 cctccattaaactgtccacctggattagaatatttaagtcagatagatcagatactgatt
  91 P  P  L  N  C  P  P  G  L  E  Y  L  S  Q  I  D  Q  I  L  I
 541 catcagcaaattgaacttctggaagttttaacaggttttgaaactaataacaaatatgaa
 111 H  Q  Q  I  E  L  L  E  V  L  T  G  F  E  T  N  N  K  Y  E
 601 attaagaacagctttggacagagggtttactttgcagcggaagatactgattgctgtacc
 131 I  K  N  S  F  G  Q  R  V  Y  F  A  A  E  D  T  D  C  C  T
 661 cgaaattgctgtgggccatctagacctttttaccttgaggattattgataatatgggtcaa
 151 R  N  C  C  G  P  S  R  P  F  T*  L  R  I  I  D  N  M  G  Q
 721 gaagtcataactctggagagaccactaagatgtagcagctgttgttgtccctgctgcctt
 171 E  V  I  T  L  E  R  P  L  R  C  S  S  C  C  C  P  C  C  L
 781 caggagatagaaatccaagctcctcctggtgtaccaataggttatgttattcagacttgg
 191 Q  E  I  E  I  Q  A  P  P  G  V  P  I  G  Y  V  I  Q  T  W
 841 cacccatgtctaccaaagtttacaattcaaaatgagaaaagagaggatgtactaaaaata
 211 H  P  C  L  P  K  F  T  I  Q  N  E  K  R  E  D  V  L  K  I
 901 agtggtccatgtgttgtgtgcagctgttgtggagatgttgattttgagattaaatctctt
 231 S  G  P  C  V  V  C  S  C  C  G  D  V  D  F  E  I  K  S  L
 961 gatgaacagtgtgtggttggcaaaatttccaagcactggactggaattttgagagaggca
 251 D  E  Q  C  V  V  G  K  I  S  K  H  W  T  G  I  L  R  E  A
1021 tttacagacgctgataactttggaatccagttccctttagaccttgatgttaaaatgaaa
 271 F  T  D  A  D  N  F  G  I  Q  F  P  L  D  L  D  V  K  M  K
1081 gctgtaatgattggtgcctgtttcctcattgacttcatgtttttgaaagcactggcagc
 291 A  V  M  I  G  A  C  F  L  I  D  F  M  F  F  E  S  T  G  S
1141 caggaacaaaaatcaggagtgtggtagtggattagtgaaagtctcctcaggaaatctgaa
 311 Q  E  Q  K  S  G  V  W  -
1201 gtctgtatattgattgagactatctaaactcatacctgtatgaattaagctgtaaggcct
1261 gtagctctggttgtatacttttgcttttcaaattatagtttatcttctgtataactgatt
1321 tataaaggtttttgtacatttttaatactcattgtcaatttgagaaaaaggacatatga
1381 gtttttgcatttattaatgaaacttcctttgaaaaactgctttaaaaaaaagtcgacgcg
1441 gccgc
```

FIG. 1A

```
   1 tctaaagactcaggaaacaaaacctaaattgcctcaaagttcaggtgcttttctccctg
  61 actttagtctagtggagtagtgcagcacctatgcctttctgagaggagtctggagagctg
 121 agtcgctgctggtgctaggattctaggaattcgcctcacttggagctgcatgagaaaaga
 181 aaggcttgcaaatggaggctcctcgctcaggaacatacttgccagctgggtatgcccctc
   1                M  E  A  P  R  S  G  T  Y  L  P  A  G  Y  A  P  Q
 241 agtatcctccagcagcagtccaaggacctccagagcatactggacgccccacattccaga
  18   Y  P  P  A  A  V  Q  G  P  P  E  H  T  G  R  P  T  F  Q  T
 301 ctaactaccaagttccccagtctggttatccaggacctcaggctagctacacagtctcaa
  38   N  Y  Q  V  P  Q  S  G  Y  P  G  P  Q  A  S  Y  T  V  S  T
 361 catctggacatgaaggttatgctgctacacggcttcctattcaaaataatcagactatag
  58   S  G  H  E  G  Y  A  A  T  R  L  P  I  Q  N  N  Q  T  I  V
 421 tccttgcaaacactcagtggatgccagcaccaccacctattctgaactgcccacctgggc
  78   L  A  N  T  Q  W  M  P  A  P  P  P  I  L  N  C  P  P  G  L
 481 tagaatacttaaatcagatagatcagcttctgattcatcagcaagttgaacttctagaag
  98   E  Y  L  N  Q  I  D  Q  L  L  I  H  Q  Q  V  E  L  L  E  V
 541 tcttaacaggctttgaaacaaataacaaatttgaaatcaagaacagcctcgggcagatgg
 118   L  T  G  F  E  T  N  N  K  F  E  I  K  N  S  L  G  Q  M  V
 601 tttatgttgcagtggaagatactgactgctgtactcgaaattgctgtgaagcgtctagac
 138   Y  V  A  V  E  D  T  D  C  C  T  R  N  C  C  E  A  S  R  P
 661 ctttcaccttaagaatcctggatcatctgggccaagaagtcatgactctggagcgacctc
 158   F  T  L  R  I  L  D  H  L  G  Q  E  V  M  T  L  E  R  P  L
 721 tgagatgcagtagctgctgcttcccctgctgcctccaggagatagaaatccaggctcctc
 178   R  C  S  S  C  C  F  P  C  C  L  Q  E  I  E  I  Q  A  P  P
 781 cgggggtgccaataggttatgtgactcagacctggcacccatgtctgccaaagctcactc
 198   G  V  P  I  G  Y  V  T  Q  T  W  H  P  C  L  P  K  L  T  L
 841 ttcagaacgacaagagggagaatgttctaaaagtagttggtccatgtgttgcatgcacct
 218   Q  N  D  K  R  E  N  V  L  K  V  V  G  P  C  V  A  C  T  C
 901 gctgttcagatattgactttgagatcaagtctcttgatgaagtgactagaattggtaaga
 238   C  S  D  I  D  F  E  I  K  S  L  D  E  V  T  R  I  G  K  I
 961 tcaccaagcagtggtctggttgtgtgaaagaggccttcacggattcggataactttggga
 258   T  K  Q  W  S  G  C  V  K  E  A  F  T  D  S  D  N  F  G  I
1021 tccaattcccgctagacctggaggtgaagatgaaagctgtgacgcttggtgcttgcttcc
 278   Q  F  P  L  D  L  E  V  K  M  K  A  V  T  L  G  A  C  F  L
1081 tcatagattacatgtttttgaaggctgtgagtaggaacagaaatccgacctgcagtagg
 298   I  D  Y  M  F  P  E  G  C  E  -
1141 aatcaatgaaagaggacagagaagatctgaagtctacacaaggagatcatatgattgaga
1201 gacctggggctttttgatttcttcattgaaatttctcagaatcaagctgttatacatgaa
1261 gcatagtatgtaacattttggttttcaaatggtagtttatcttttacattattggaatag
1321 acctggataattatctttatacacttctaaaaatatgcaccaaattcaagttaaaaaaaa
1381 aaagacgaagagaagtgtatgttttaaaataaaacattttatggaaaagtaagttaaatc
1441 ataatctgggatttatttttcatcttttgttcaatttaaaccttgttagtgctgatttta
1501 ttataaaattgtactttactatcaaacctagttagtttatttcttacagaaatcctccta
1561 ttattttgaaattacatatttttgaaagctttttaaaagatactattgcctgggaaattc
1621 ta
```

FIG. 1B

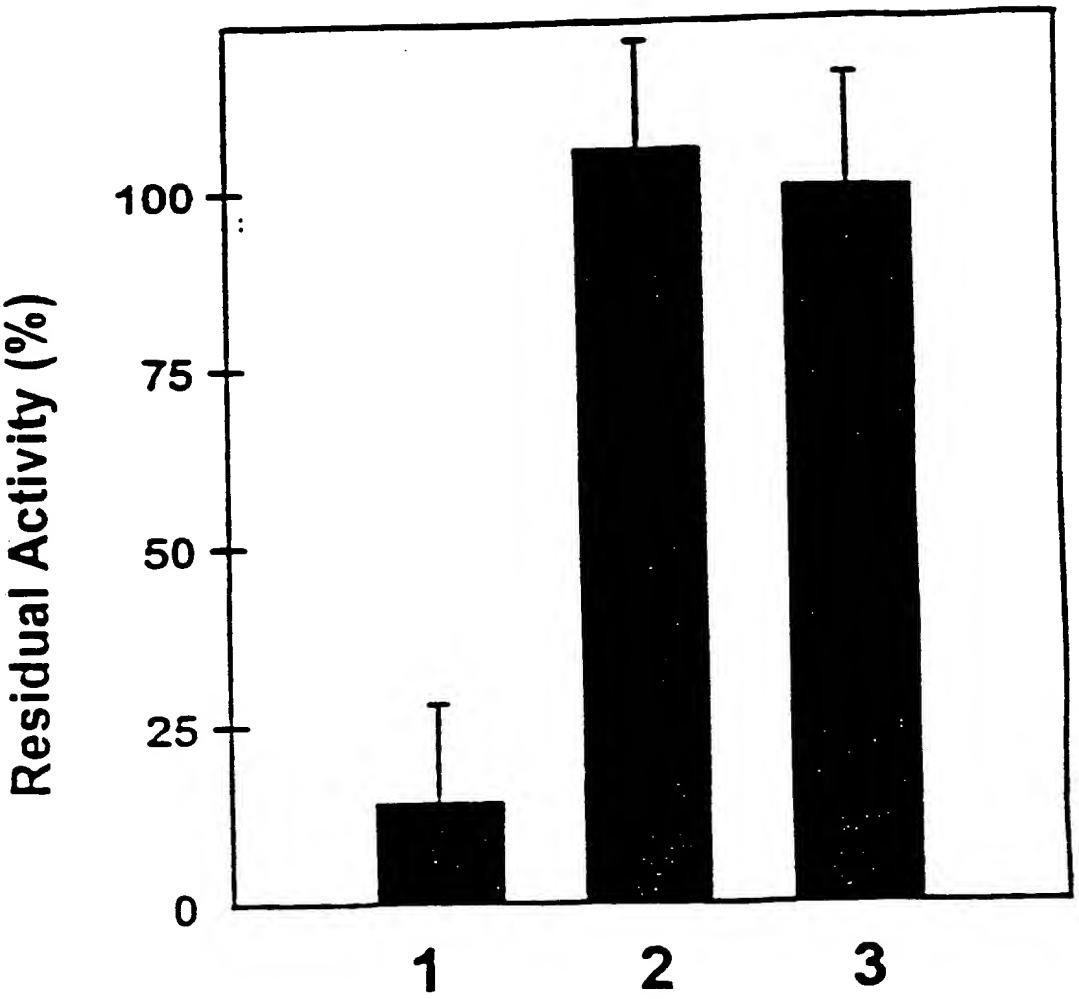


FIG. 2

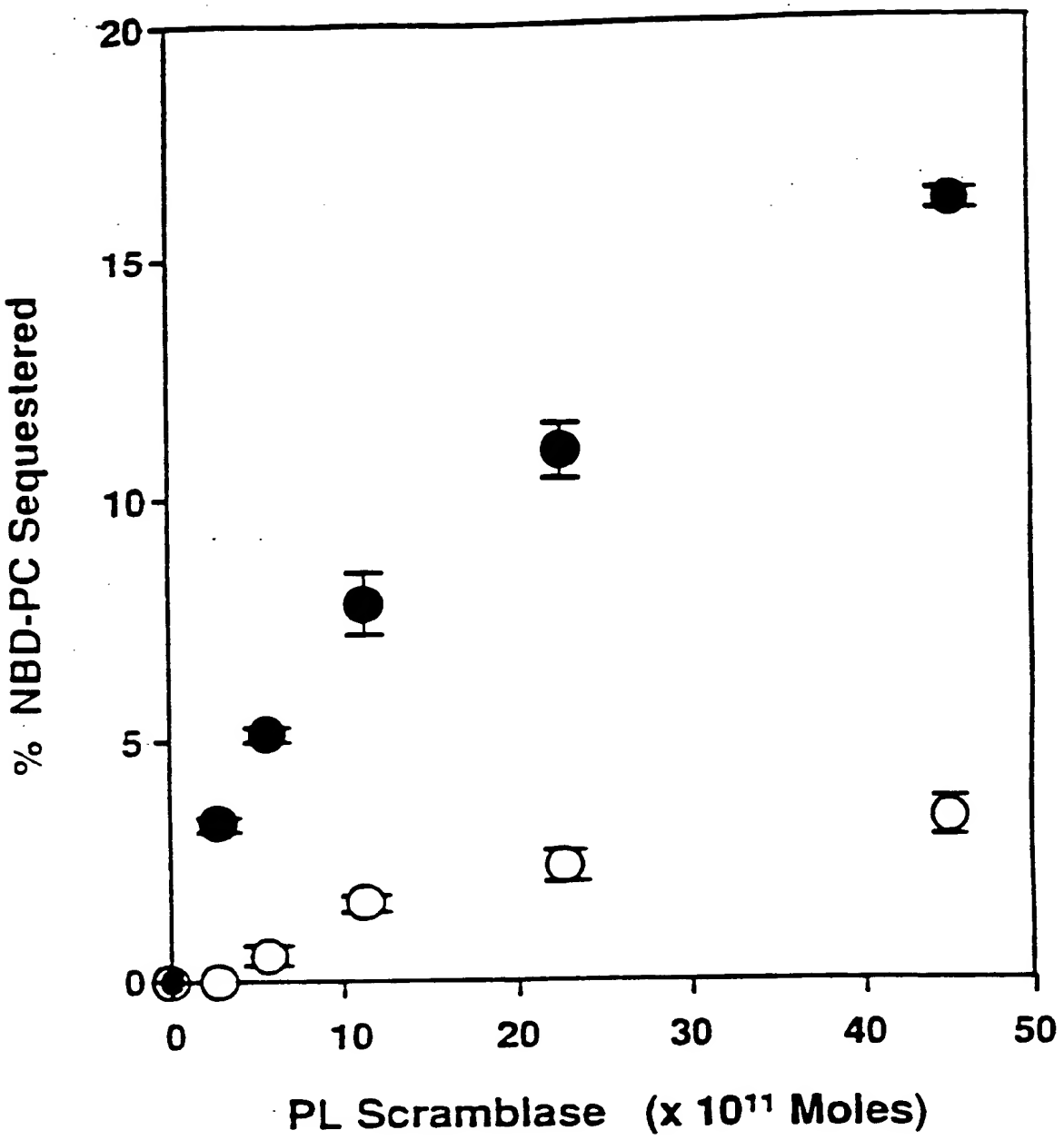

20
15
10
5
0
% NBD-PC Sequestered
0
10
20
30
40
50
PL Scramblase (x 10¹¹ Moles)

FIG. 3

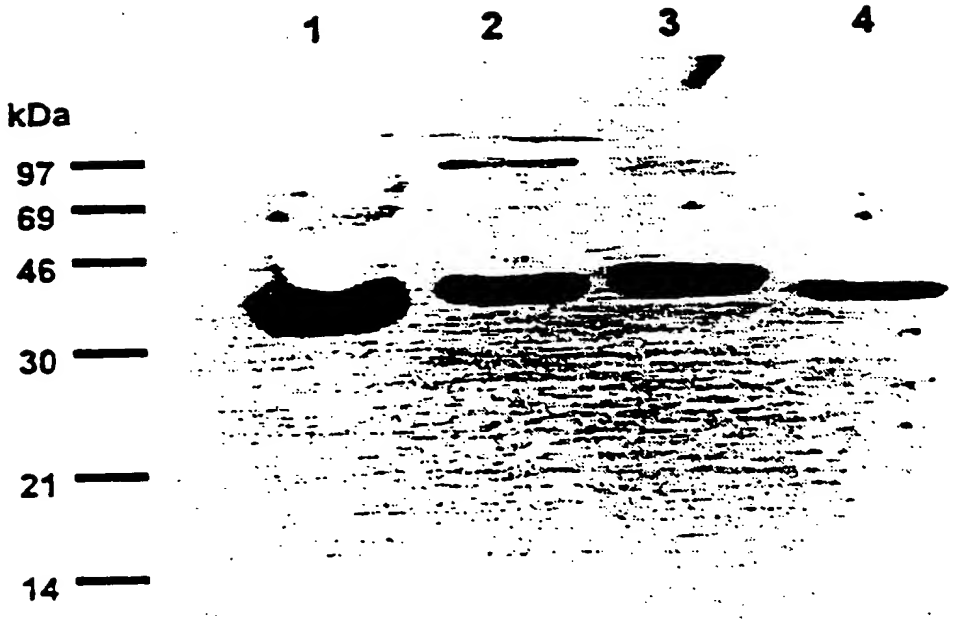


FIG. 4

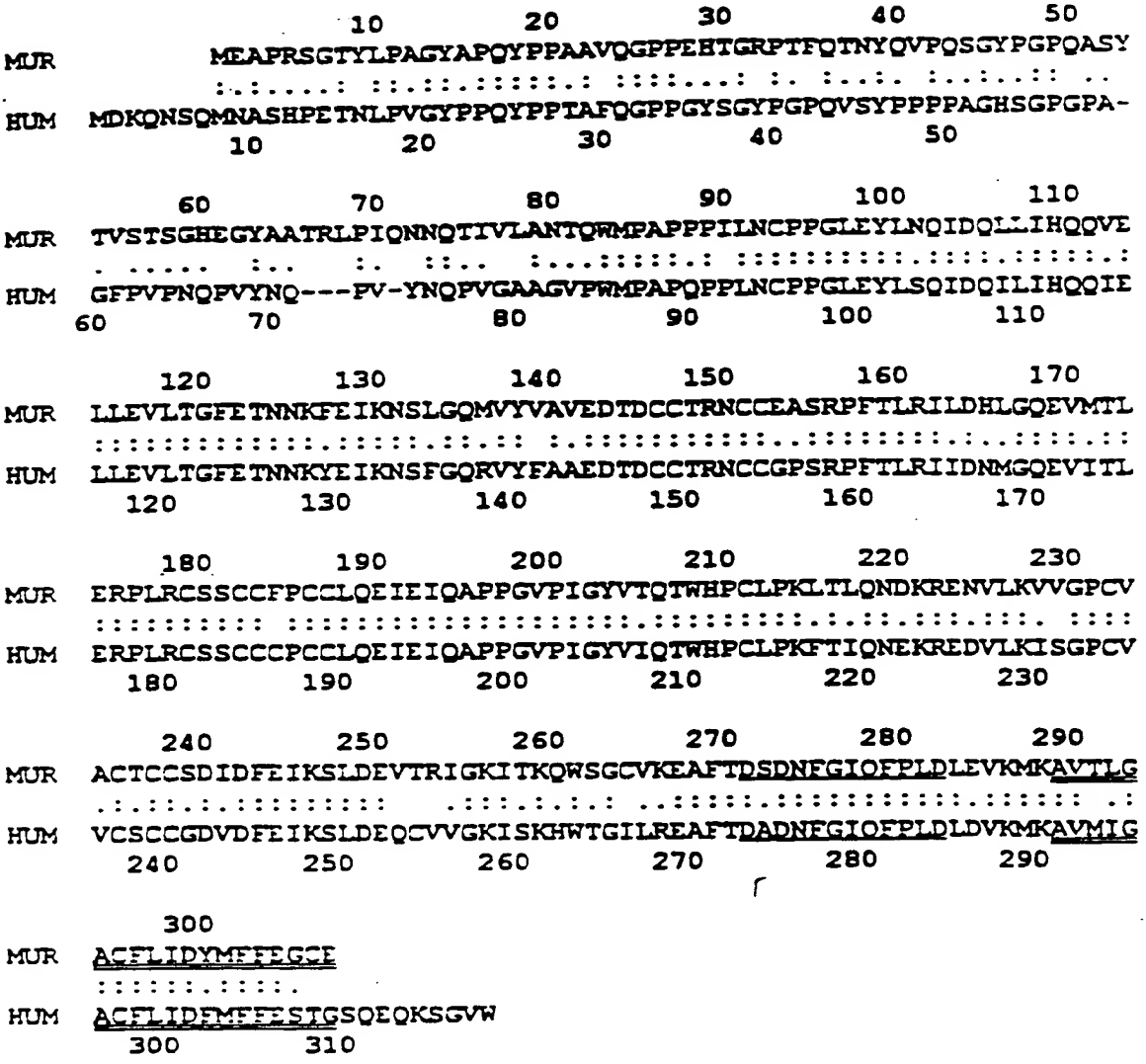

MUR MEAPRSGTYLPAGYAPQYPPAAVQGPPEHTGRPTFQTNYQVPQSGYPGPQASY
HUM MDKQNSQMNASHPETNLPVGYPPQYPPTAFQGPPGYSGYPGPQVSYPPPPAGHSGPGPA-
MUR TVSTSGHEGYAATRLPIQNNQTIVLANTQWMPAPPPILNCPPGLEYLNQIDQLLIHQQVE
HUM GFPVPNQPVYNQ---PV-YNQPVGAAGVPWMPAPQPPLNCPPGLEYLSQIDQILIHQQIE
MUR LLEVLTGFETNNKFEIKNSLGQMVYVAVEDTDCCTRNCCEASRPFTLRILDHLGQEVMTL
HUM LLEVLTGFETNNKYEIKNSFGQRVYFAAEDTDCCTRNCCGPSRPFTLRIIDNMGQEVITL
MUR ERPLRCSSCCFPCCLQEIEIQAPPGVPIGYVTQTWHPCLPKLTLQNDKRENVLKVVGPCV
HUM ERPLRCSSCCCPCCLQEIEIQAPPGVPIGYVIQTWHPCLPKFTIQNEKREDVLKISGPCV
MUR ACTCCSDIDFEIKSLDEVTRIGKITKQWSGCVKEAFTDSDNFGIQFPLDLEVKMKAVTLG
HUM VCSCCGDVDFEIKSLDEQCVVGKISKHWTGILREAFTDADNFGIQFPLDLDVKMKAVMIG
MUR ACFLIDYMFFEGCE
HUM ACFLIDFMFFESIGSQEQKSGVW
10 20 30 40 50
60 70 80 90 100 110
120 130 140 150 160 170
180 190 200 210 220 230
240 250 260 270 280 290
300 310

FIG. 5

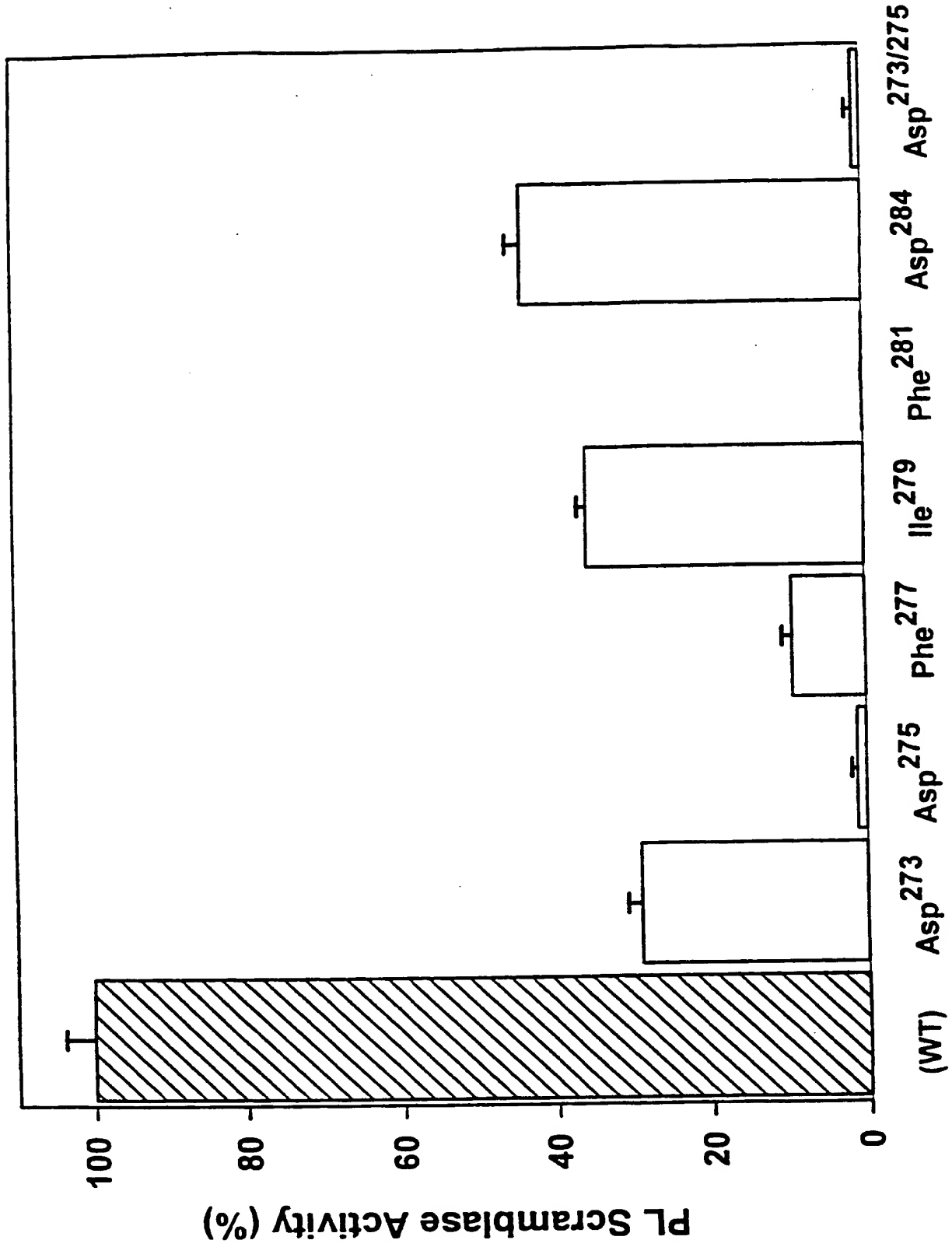

PL Scramblase Activity (%)
0
20
40
60
80
100
(WT)
Asp273
Asp275
Phe277
Ile279
Phe281
Asp284
Asp273/275

FIG. 6

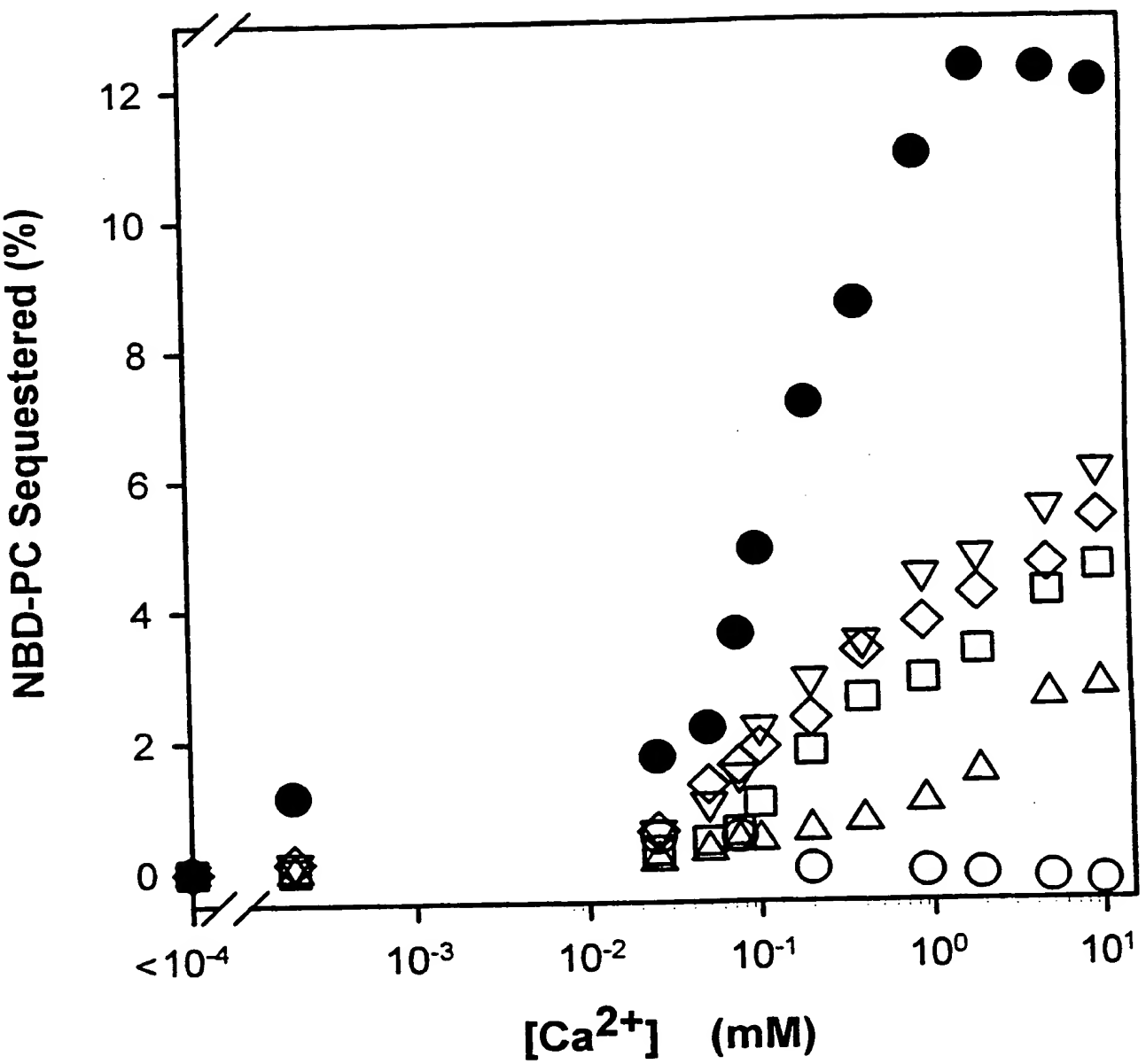


FIG. 7

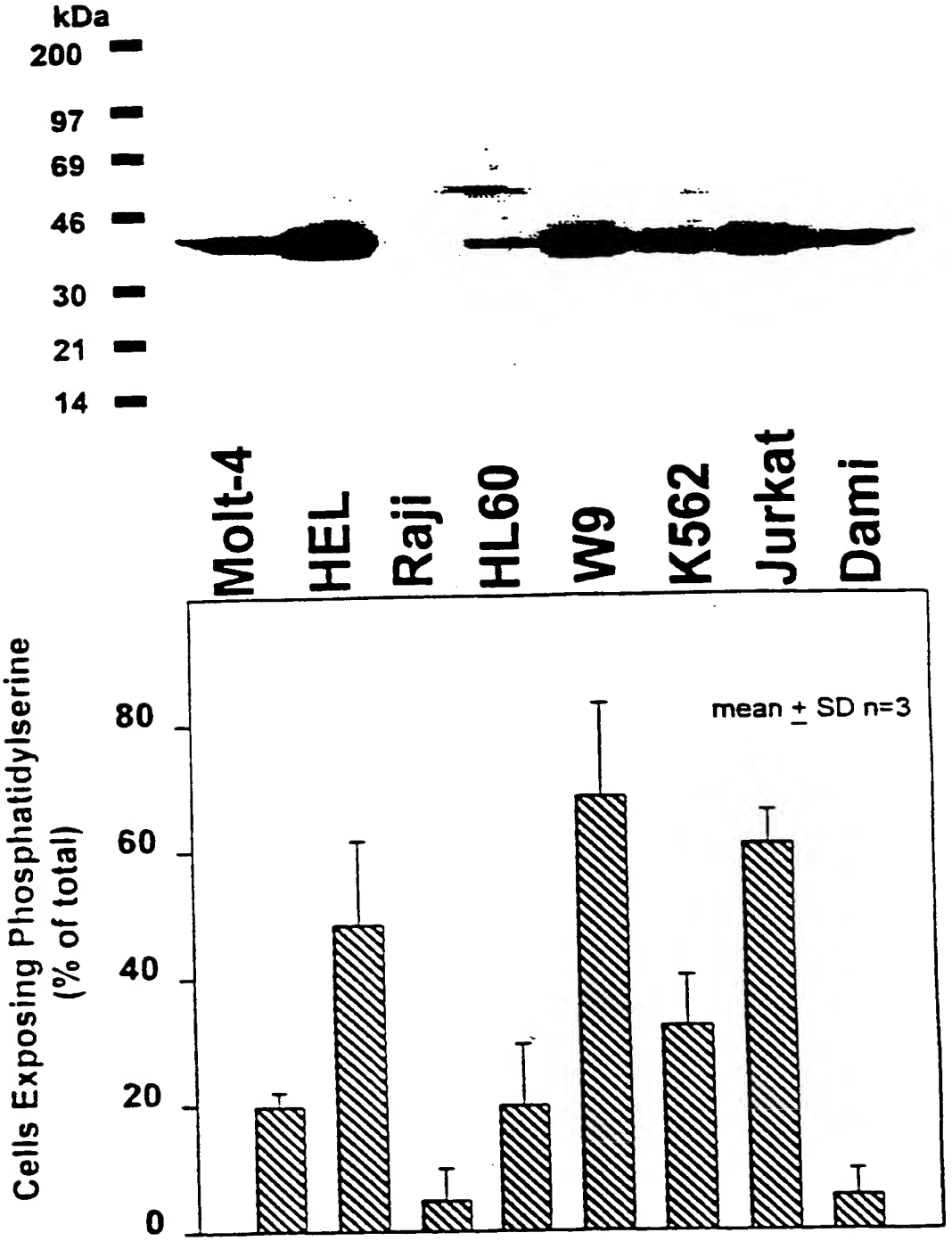

kDa
200
97
69
46
30
21
14
Molt-4
HEL
Raji
HL60
W9
K562
Jurkat
Dami
Cells Exposing Phosphatidylserine
(% of total)
80
60
40
20
0
mean ± SD n=3

FIG. 8

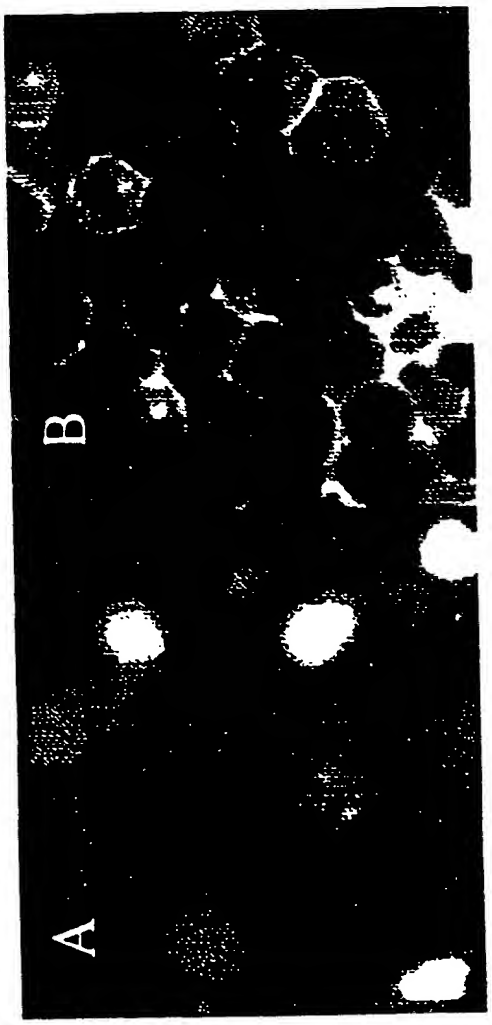


FIG. 9

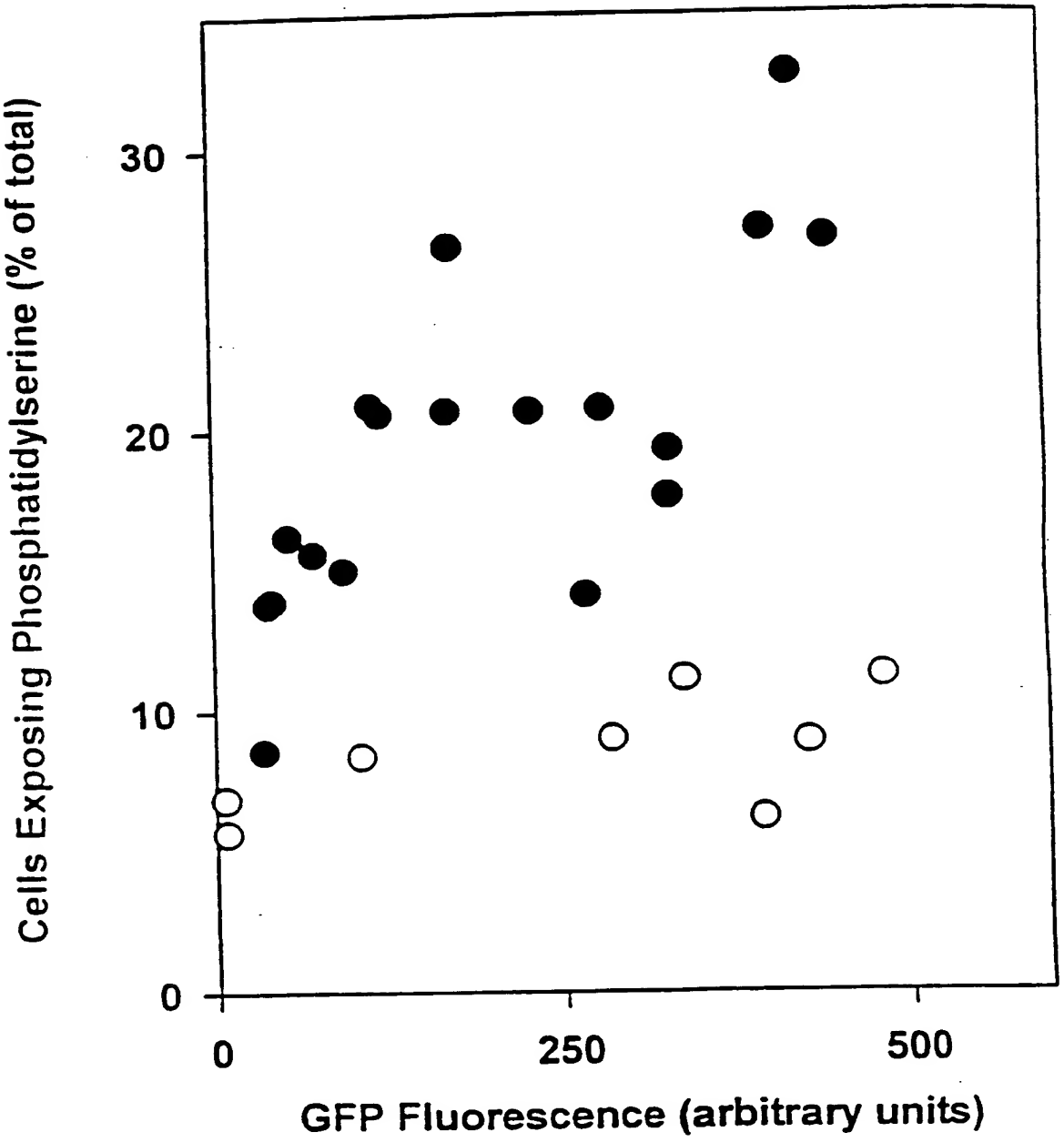

Cells Exposing Phosphatidylserine (% of total)
30
20
10
0
0
250
500
GFP Fluorescence (arbitrary units)

FIG. 10

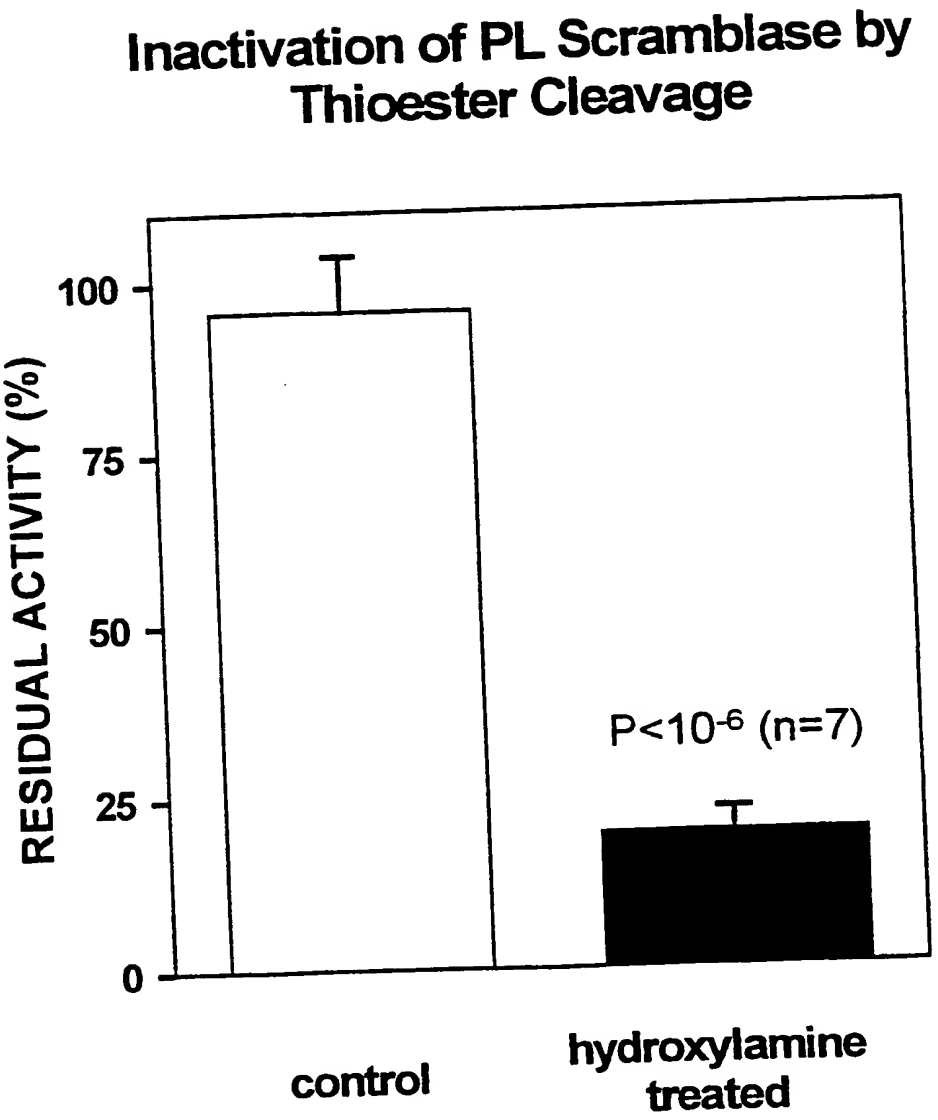

Inactivation of PL Scramblase by Thioester Cleavage
RESIDUAL ACTIVITY (%)
100
75
50
25
0
P<10-6 (n=7)
control
hydroxylamine treated

FIG. 11

Metabolic Labeling of PL Scramblase with [^{3}H]-Palmitate Reveals Covalent Thioester-Linked Fatty Acid

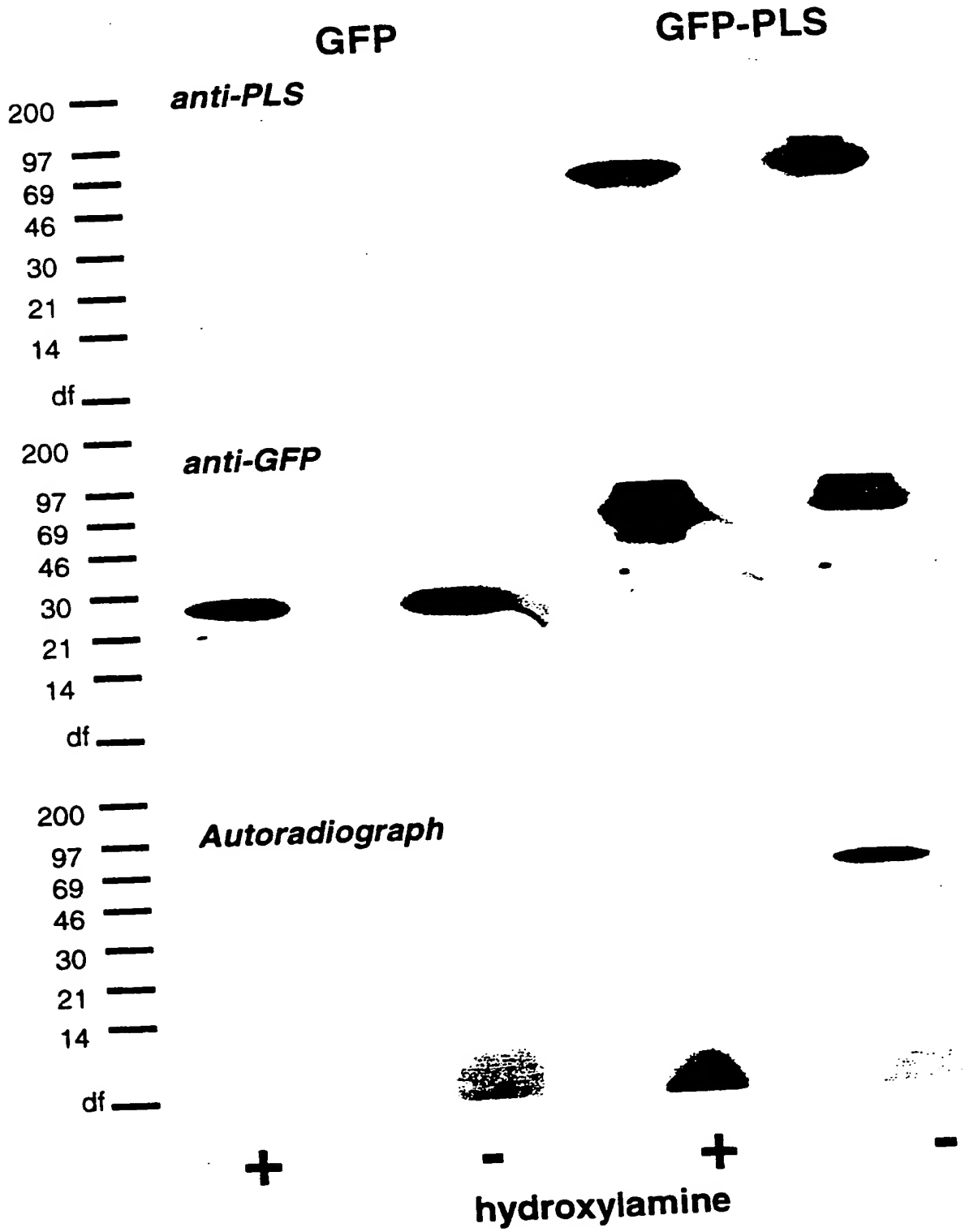


FIG. 12

TLC Analysis of [^{3}H]-Fatty Acid From Hydroxylamine-Treated PL Scramblase

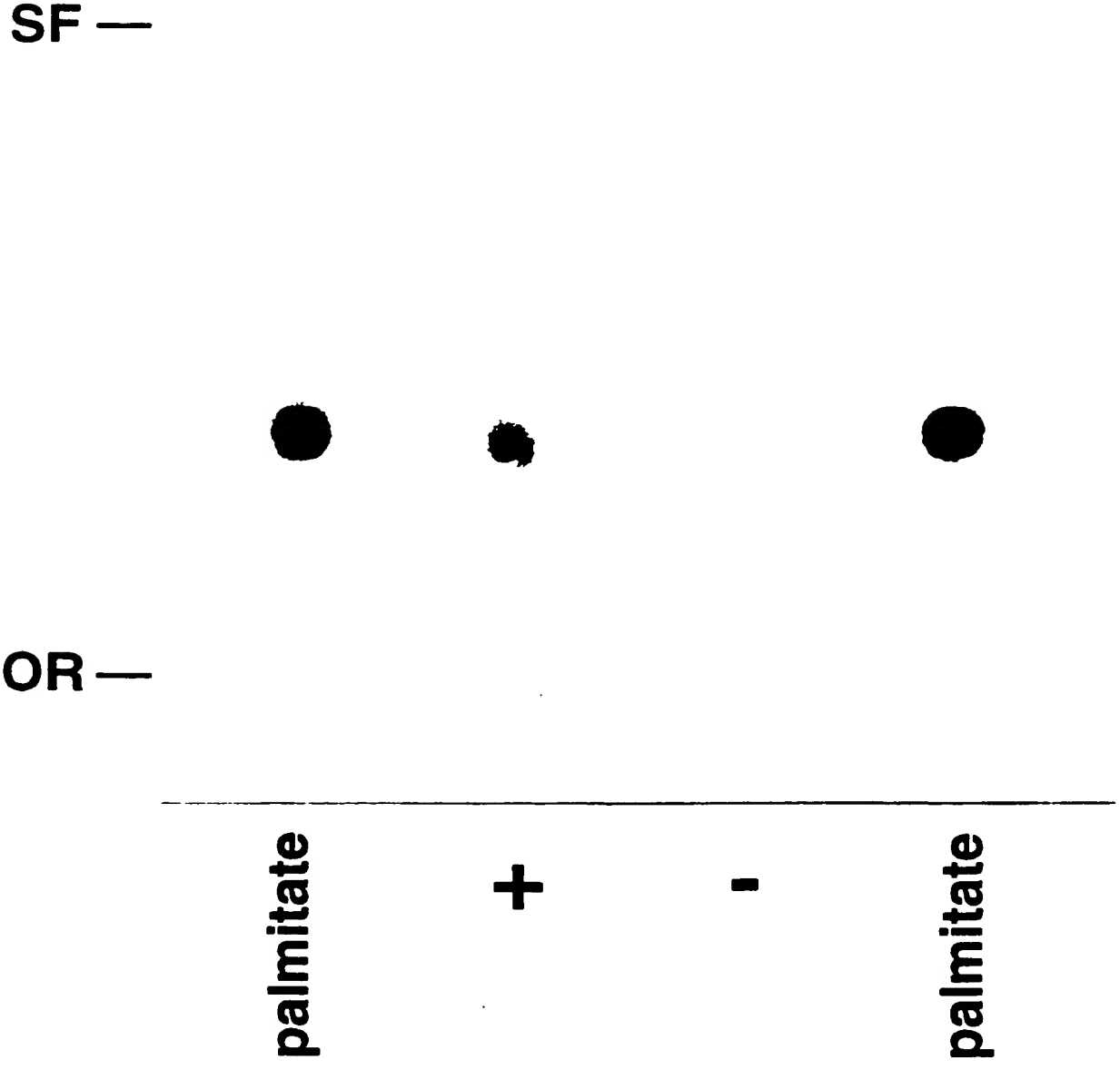


FIG. 13

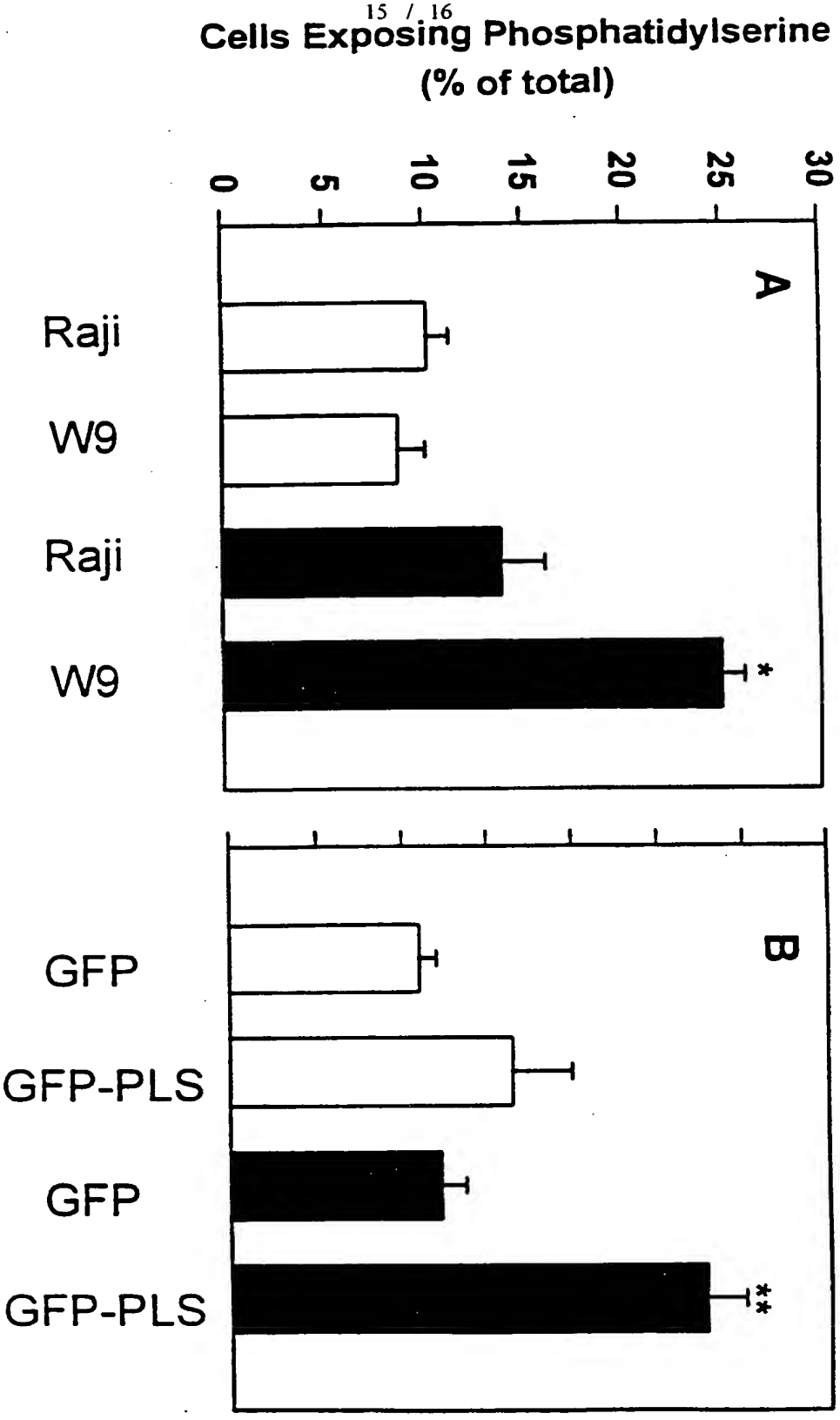
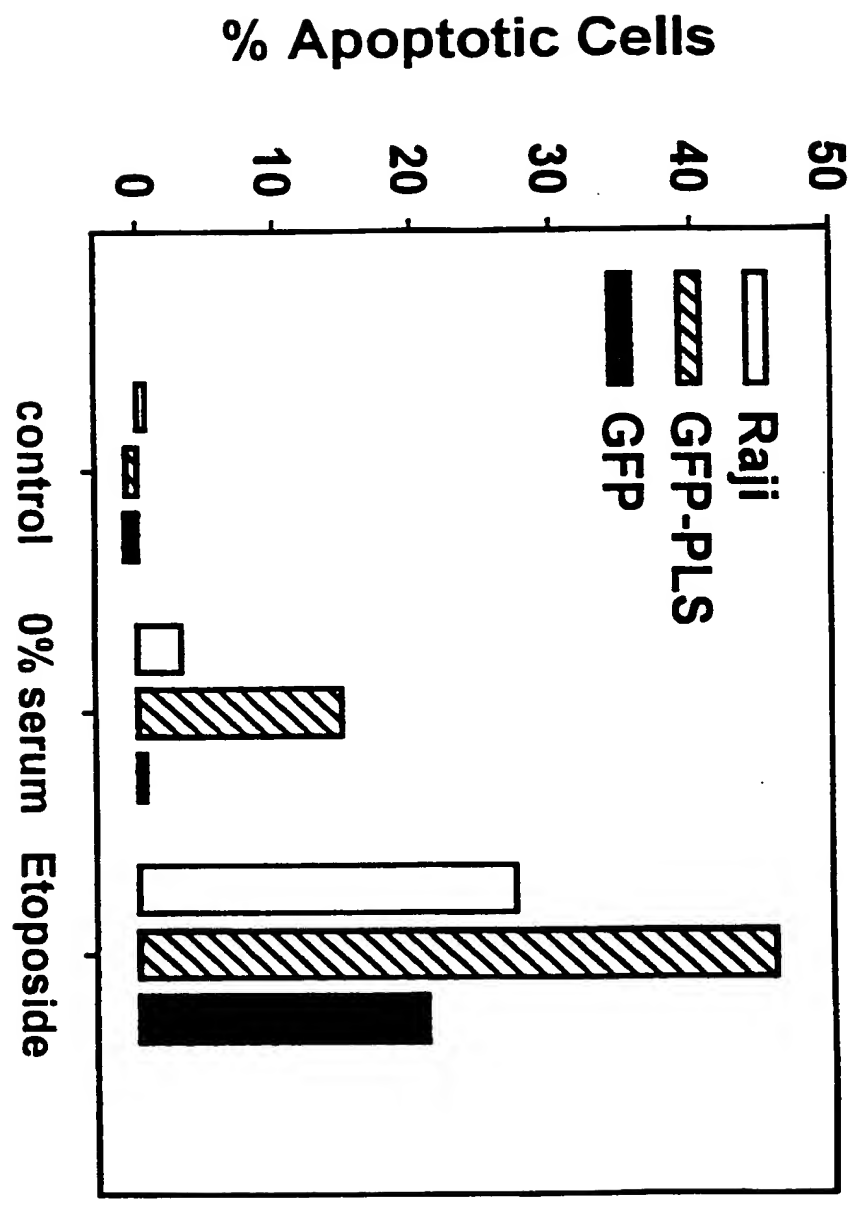

Cells Exposing Phosphatidylserine
(% of total)
0
5
10
15
20
25
30
A
Raji
W9
Raji
W9
*
B
GFP
GFP-PLS
GFP
GFP-PLS
**

FIG. 14



Transfection With cDNA Encoding PL Scramblase Increases Apoptotic Response of Human B-Lymphoma Line Raji

FIG. 15